DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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JUL 20 2001

Peter S. Reichertz, Esquire
Arent Fox Kintner Plotkin & Kahn
1050 Connecticut Avenue, NW
Washington, DC 20036-5339

Re: Docket No. 78N-036L
Comment Nos. CP20 and C205

Dear Mr. Reichertz:

This is in reference to your citizen petition dated June 9, 1995, submitted on behalf of the C. B. Fleet Company, Inc., and filed in FDA's Dockets Management Branch as Comment No. CP20 under Docket No. 78N-036L. The petition requested an amendment of the tentative final monograph for over-the-counter (OTC) laxative drug products (50 FR 2124) to allow for use of a large volume tap water enema as the final cleansing step, in lieu of a bisacodyl suppository or enema, in bowel cleansing systems for two preparations, Fleet®Prep Kit 2 and Fleet®Prep Kit 5. In letters filed under Docket No. 78N-036L, dated December 13, 1999 (Comment No. LET182) and September 23, 2000 (Comment No. LET183), the Division of OTC Drug Products requested additional information to complete our evaluation of the citizen petition. The additional information was submitted on November 14, 2000 (Comment No. 205 under Docket No. 78N-036L).

In your November 14, 2000 letter, you noted that the C. B. Fleet Company, Inc. has discontinued Fleet®Prep Kit 5 which contained 3 laxative drug products for sequential administration as follows: magnesium citrate powder for reconstitution, oral bisacodyl, and a large volume tap water enema. Therefore, you requested that CP 20 be amended to only consider the Fleet ®Prep Kit 2, which consists of 1 Fleet®Phospho-Soda® (Sodium Phosphates Oral Solution), 4 Fleet® Bisacodyl Tablets, and 1 Fleet® Bagenema®. The Fleet ®Prep Kit 2 would be used sequentially in the order stated above and the indication would be "for use as a bowel cleansing regimen in preparing patients for surgery or for preparing the colon for x-ray or endoscopic examination." You stated that the Bagenema® is marketed as an enema kit device pursuant to 21 CFR 876.5210 intended for the instillation of water or other fluids into the colon through a nozzle inserted into the rectum to promote evacuation of the contents of the lower colon. You concluded that, in accordance with 21 CFR 876.5210, the use of a tap water enema as a medical device is recognized by the agency as a safe and effective means of evacuating the contents of the colon.

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The agency has reviewed all of the information provided and determined that it does not support your citizen petition request. Therefore, the agency is denying your request to amend the OTC laxative tentative final monograph to include the components of the Fleet ®Prep Kit 2 for the indication "for use as a bowel cleansing regimen in preparing patients for surgery or for preparing the colon for x-ray or endoscopic examination."

The reference articles submitted did not address the components of the Fleet ®Prep Kit 2. The manufacturer has not compared nor submitted literature that compares different volumes of tap water in different populations to determine the most appropriate volume to use. The petition does not provide data that demonstrate how much water is needed for a tap water enema with the Fleet ®Prep Kit 2 and the diagnostic procedure for which a given volume is appropriate. There were no data that evaluated the rationale for selection and timing of the ingredients used in Fleet ®Prep Kit 2 for each type of bowel procedure, nor were there any data to clarify where a tap water enema should be administered and by whom it should be administered. Some of the literature supported use of the enema in the radiology suite by trained personnel.

We have the following specific comments on your client's responses to the Division's request for data.

Request 1. Submit data demonstrating how much water is safe for administration of a tap water enema, including demographic and medical information about the population studied.

The manufacturer submitted reference information from 10 medical textbooks that used a cleansing tap water enema as a final cleansing step and 24 references from the medical literature that described a variety of bowel cleansing systems. The references in general did not address the safety of tap water enemas nor the specific or best volume to be used. None of the preparations used were identical to the Fleet® Prep Kit 2. The reference articles did not address the specific components included in Fleet® Prep Kit 2. Thus, the safety and efficacy of the Fleet ®Prep Kit 2 could not be evaluated. The demographic population information was also lacking. Safety issues were not addressed in most of the reference material. Several reference articles pointed out adverse events associated with tap water enemas such as septic shock, perforation of the rectum by the rectal enema tips, colon perforations, water intoxication, and electrolyte abnormalities. The danger of high water temperatures of tap water enemas was also mentioned in one article. Several reference articles noted that trained personnel and not the consumer should give the tap water enemas.

Request 2. Submit data demonstrating how much water is needed for a tap water enema with your client's kit(s) and the diagnostic procedure for which the volume(s) are appropriate.

There were 6 reference articles submitted in response to this request. None of the articles studied the components used in the Fleet Prep Kit 2.

Request 3. Submit any new data that may be available for the kits, either from clinical trials, literature, or safety databases.
The manufacturer stated that all new information has been submitted in response to the other questions. We note there were no clinical trials submitted that specifically tested the Fleet®Prep Kit 2 and the use of tap water enemas.

Request 4. Submit the rationale for selection and timing of the ingredients used in the kits.
There were no data to support the safety and efficacy of the stated rationale for the selection and timing of the ingredients in the Fleet® Prep Kit 2.

Request 5. Submit the total number of kits that have been sold since the product was first marketed and all adverse reports received regarding the kits.
The spontaneous reports of adverse events submitted do not demonstrate a major safety problem with Fleet® Prep Kit 2. One of these reports is an adverse event associated with the device, not with the drugs or tap water enema. We note that adverse events associated with OTC drug products not subject to the new drug application approval process are vastly underreported, because there are no mandatory reporting requirements. Voluntary reporting normally accounts for only about 10% of all reports. Therefore, these reports may provide only a general overview of safety, but because of underreporting they do not provide substantial evidence of safety.

Request 6. Submit all adverse reports for the enema bag, whether it was sold alone or as part of a kit.
The number of spontaneous reports of adverse events submitted to the manufacturer for the Bagenema® primarily appear to be due to problems with ragged nozzle tips of tubing causing rectal irritation and consumers not removing the protective shield on the nozzle tip before inserting the tip into the rectum. See also Request 7 below.

Request 7. Submit all consumer and professional warnings and directions for your client's kits (including use of the enema bag) that will assure us that these products are adequately labeled and safe for the target population.
We believe that the labeling for consumer use should be as complete as the professional labeling. We note that in one of the Bagenema samples included in the submission one plastic nozzle tip had a ragged tip. Manufacturers need to ensure that the nozzle tips are very smooth to avoid injury to the rectal mucosa and that there are adequate warnings and directions for safe use. Manufacturers should consider including a diagram depicting how to remove the protective shield from the enema tip before use.

Request 8. Submit any data or other information you have to support where and by whom the tap water enema should be administered.
The manufacturer submitted 13 articles in response to this request. None of the Prep Kits used in the articles were the same components as the Fleet ®Prep Kit 2. Some articles did not study the use of tap water enemas. Most of the enemas were administered in the hospital, and the articles did not indicate who administered the enemas. Other articles stated that tap water enemas are best administered by professionals in radiology suites or

in hospitals, and not self-administered at home. One article pointed out that in the elderly there may be hemodynamic complications of bowel preparations.

Request 9. Submit samples of the complete kits as they are currently marketed including all consumer and professional labeling and other information that may be available for use with the kits.
The currently submitted consumer and professional labeling will need significant revision to provide adequate information for use, specifically addressing warnings and directions. The agency will be addressing professional labeling for these kits in the future.

In conclusion, your petition does not contain adequate information to support the safety and effectiveness of the Fleet® Prep Kit 2 for its intended use. Further, the listing of an enema kit in 21 CFR 876.5210 does not establish the safety and effectiveness of the Bagenema® as a component of the Fleet® Prep Kit 2 bowel cleansing system. Specific data are needed to support its use as part of the bowel cleansing system.

For the reasons stated above, the agency is denying your petition. Any comment that you wish to make on the above information should be submitted in triplicate, identified with the docket and comment numbers shown at the beginning of this letter to the Dockets Management Branch (HFA-305) Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852.

Sincerely yours,

Dennis E. Baker
Associate Commissioner
for Regulatory Affairs

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 7.25.01

FROM: Director
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 78N-036L

TO: Dockets Management Branch, HFA-305

[X] The attached material should be placed on public display under the above referenced Docket No.

[X] This material should be cross-referenced to Comment No. CP20

Charles J. Ganley, M.D.

Attachment